

Amendments to the Claims:

1-4 (Canceled)

5. (Currently Amended) A pharmaceutical composition having a pH of about 3.0 to about 5.0 and comprising interferon-beta (IFN- β), wherein said composition is prepared by a method consisting essentially of:

- a) denaturing IFN- β with guanidine hydrochloride (HCl);
- b) renaturing the IFN- β via dilution into a first buffer to obtain a renatured IFN- β solution comprising residual guanidine HCl; and
- c) removing said residual guanidine HCl from said renatured IFN- β solution by diafiltration or dialysis of said renatured IFN- β solution into a second buffer that is pharmaceutically acceptable, wherein said second buffer is selected from the group consisting of ~~glycine~~, aspartic acid, and sodium succinate.

6. (Previously Presented) The pharmaceutical composition of claim 5, wherein said first buffer has a pH of about 3.0 to about 5.0, and wherein said residual guanidine HCl is present in said renatured IFN- β solution at a concentration of 1.6 M or less.

7. (Previously Presented) The pharmaceutical composition of claim 6, wherein said first buffer has a pH of about 3.0 to about 4.0, and wherein said residual guanidine HCl is present in said renatured IFN- β solution at a concentration of 0.2 M or less.

8. (Previously Presented) The pharmaceutical composition of claim 7, wherein said first buffer has a pH of about 3.0, and wherein said residual guanidine HCl is present in said renatured IFN- β solution at a concentration of 0.1 M or less.

9. (Previously Presented) The pharmaceutical composition of claim 5, wherein said composition comprises substantially monomeric IFN- β .

10-12 (Canceled)

13. (Currently Amended) A pharmaceutical composition having a pH of about 3.0 to about 5.0 and comprising interferon-beta (IFN- β), wherein said composition is prepared by a method consisting essentially of:

- a) obtaining a sample comprising substantially purified IFN- β ;
- b) mixing said sample with guanidine hydrochloride (HCl) to obtain a first solution comprising solubilized denatured IFN- β ;
- c) diluting said first solution into a first buffer to obtain a second solution comprising solubilized renatured IFN-beta and residual guanidine HCl; and
- d) removing residual guanidine HCl from said second solution by diafiltration or dialysis of said second solution into a second buffer that is pharmaceutically acceptable, wherein said second buffer is selected from the group consisting of ~~glycine~~, aspartic acid, and sodium succinate.

14. (Previously Presented) The pharmaceutical composition of claim 13, wherein said composition comprises substantially monomeric IFN- β .

15. (Previously Presented) The pharmaceutical composition of claim 13, wherein said first buffer has a pH of about 3.0 to about 5.0, and wherein said residual guanidine HCl is present in said second solution at a concentration of 1.6 M or less.

16. (Previously Presented) The pharmaceutical composition of claim 15, wherein said first buffer has a pH of about 3.0 to about 4.0, and wherein said residual guanidine HCl is present in said second solution at a concentration of 0.2 M or less.

17. (Previously Presented) The pharmaceutical composition of claim 16, wherein said first buffer has a pH of about 3.0, and wherein said residual guanidine HCl is present in said second solution at a concentration of 0.1 M or less.

18. (Canceled)

19. (Currently Amended) A composition comprising substantially monomeric interferon-beta (IFN- β) and having a pH of about 3.0 to about 5.0, wherein said composition is prepared by a method consisting essentially of:

- a) preparing a sample comprising substantially purified IFN- β ;
- b) mixing said sample with guanidine hydrochloride (HCl) to obtain a first solution comprising solubilized denatured IFN- β ; and
- c) renaturing said IFN- β by dilution of said first solution with a buffer, wherein said buffer has a pH of about 3.0 to about 5.0 and is selected from the group consisting of ~~glycine~~, aspartic acid, and sodium succinate.

20. (Previously Presented) A pharmaceutical composition comprising the composition of claim 19.

21-25 (Canceled)

26. (Previously Presented) The pharmaceutical composition of claim 5, wherein said IFN- β has the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2.

27. (Previously Presented) The pharmaceutical composition of claim 5, wherein said IFN- β is glycosylated or unglycosylated.

28. (Previously Presented) The pharmaceutical composition of claim 5, wherein said IFN- β is recombinantly produced.

29. (Previously Presented) The pharmaceutical composition of claim 5, wherein said IFN- β has at least 80% amino acid sequence identity with the amino acid sequence set forth in

Appl. No.: 10/035,420
Amendment. Dated September 27, 2005
Reply to Office Action of June 27, 2005

SEQ ID NO:1 as calculated using the ALIGN program with a PAM 120 weight residue table, a gap length penalty of 12, and a gap penalty of 4.

30. (Previously Presented) The pharmaceutical composition of claim 5, wherein said composition is injectable.

31. (Previously Presented) The pharmaceutical composition of claim 13, wherein said IFN- β has the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2.

32. (Previously Presented) The pharmaceutical composition of claim 13, wherein said IFN- β is glycosylated or unglycosylated.

33. (Previously Presented) The pharmaceutical composition of claim 13, wherein said IFN- β is recombinantly produced.

34. (Previously Presented) The pharmaceutical composition of claim 13, wherein said IFN- β has at least 80% amino acid sequence identity with the amino acid sequence set forth in SEQ ID NO:1 as calculated using the ALIGN program with a PAM 120 weight residue table, a gap length penalty of 12, and a gap penalty of 4.

35. (Previously Presented) The pharmaceutical composition of claim 13, wherein said composition is injectable.

36. (Currently Amended) The composition of claim 5, wherein said first buffer is selected from the group consisting of ~~glycine~~, aspartic acid, and sodium succinate.

37. (Currently Amended) The composition of claim 13, wherein said first buffer is selected from the group consisting of ~~glycine~~, aspartic acid, and sodium succinate.

38. (Previously Presented) The composition of claim 19, wherein said IFN- β has the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2.

39. (Previously Presented) The composition of claim 19, wherein said IFN- β is glycosylated or unglycosylated.

40. (Previously Presented) The composition of claim 19, wherein said IFN- β is recombinantly produced.

41. (Previously Presented) The composition of claim 19, wherein said IFN- β has at least 80% amino acid sequence identity with the amino acid sequence set forth in SEQ ID NO:1 as calculated using the ALIGN program with a PAM 120 weight residue table, a gap length penalty of 12, and a gap penalty of 4.

42. (Currently Amended) A pharmaceutical composition having a pH of about 3.0 to about 5.0 and comprising interferon-beta (IFN- β), wherein said composition is prepared by a method consisting essentially of:

- a) denaturing IFN- β with guanidine hydrochloride (HCl);
- b) renaturing the IFN- β via dilution into a first buffer to obtain a renatured IFN- β solution comprising residual guanidine HCl, wherein said first buffer has a pH of about 3.0 to about 5.0 and is selected from the group consisting of ~~glycine~~, aspartic acid, and sodium succinate; and
- c) removing said residual guanidine HCl from said renatured IFN- β solution by diafiltration or dialysis of said renatured IFN- β solution into a second buffer that is pharmaceutically acceptable, wherein said second buffer is selected from the group consisting of ~~glycine~~, aspartic acid, and sodium succinate.

43. (Previously Presented) The pharmaceutical composition of claim 42, wherein said composition comprises substantially monomeric IFN- β .

44. (Canceled)

45. (Currently Amended) The pharmaceutical composition of claim ~~44~~42, wherein said second buffer is aspartic acid.

46. (Previously Presented) The pharmaceutical composition of claim 42, wherein said IFN- β has the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2.

47. (Previously Presented) The pharmaceutical composition of claim 42, wherein said IFN- β is glycosylated or unglycosylated.

48. (Previously Presented) The pharmaceutical composition of claim 42, wherein said IFN- β is recombinantly produced.

49. (Previously Presented) The pharmaceutical composition of claim 42, wherein said IFN- β has at least 80% amino acid sequence identity with the amino acid sequence set forth in SEQ ID NO:1 as calculated using the ALIGN program with a PAM 120 weight residue table, a gap length penalty of 12, and a gap penalty of 4.